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February 27, 2003

VIA EXPRESS MAIL

Commissioner for Patents
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Re: U.S. Patent Application No.: 09/945325
For: NOVEL AUTOINDUCER MOLECULES AND USES THEREFOR
Inventors: Pesci, Everett C. *et al.*
Filed: August 31, 2001
Our Ref. No.: UIZ-068CP

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form 1449;
3. Copies of references cited in PTO Form 1449 (120);
4. A copy of the International Search Report; and
5. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

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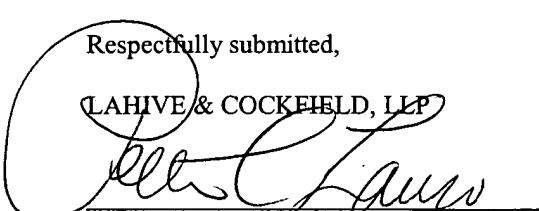
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Respectfully submitted,

LAHIVE & COCKFIELD, LLP



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In re the application of: Pesci, Everett C. *et al.*

Serial No.: 09/945325

Filed: August 31, 2001

For: NOVEL AUTOINDUCER MOLECULES AND
USES THEREFOR

Attorney Docket No.: UIZ-068CP

Group Art Unit: 1625

Examiner: Huang, Evelyn Mei

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Washington, D.C. 20231

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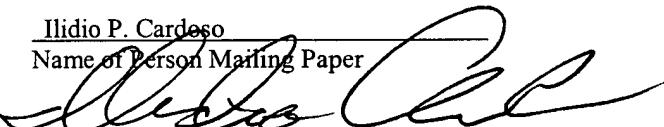
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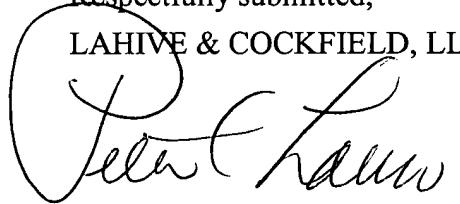
Applicants and their Attorney are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. Reference ID Nos. A6, A12, A14, A16, A17, A21, A22, A23, B2, B6, B10, B14, C2, C3, D7, D9, E1, E13, and F6 were cited in an International Search Report during the prosecution of PCT/US01/27165 which corresponds to the above referenced application. A copy of the report and each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

In accordance with 37 CFR §1.97(d)(2) and §1.17(p), please charge the \$180.00 submission fee to our Deposit Order Account No. 12-0080. Please charge any necessary additional fees or credit any overpayments to our Deposit Order Account No. 12-0080.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP



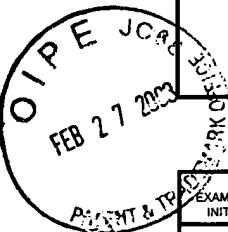
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Date: February 27, 2003

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Enclosures

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO UIZ-068CP	SERIAL NO. 09/945325
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT	Pesci, Everett C. et al.	
		FILING DATE August 31, 2001	GROUP 1625	



U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	4,650,750	03/87	Giese	435	7	TECH CENTER 1600 REC'D FEB 21 2002
	A2	4,709,016	11/87	Giese	530	389	MAR 6 1990
	A3	5,239,088	08/93	Hoffman et al.	549	321	REC'D
	A4	5,320,805	06/94	Kramer et al.	422	28	REC'D
	A5	5,536,750	06/96	deSolms et al.	514	538	REC'D
	A6	5,591,872	01/97	Pearson et al.	549	321	REC'D
	A7	5,593,827	01/97	Bycroft et al.	435	6	REC'D
	A8	5,686,472	11/97	Anthony et al.	514	357	
	A9	5,776,974	07/98	Bycroft et al.	514	445	
	A10	6,337,347	01/02	Livinghouse	514	471	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
	A11	JP 58096079	06/83	Japan			Abstract Only
	A12	JP 59051267	03/84	Japan			Abstract Only
	A13	JP 60045568	03/85	Japan			Abstract Only
	A14	EP 0 177 764 A1	05/85	EPO			
	A15	WO 92/18614 A1	10/92	WO			
	A16	JP 07188208	07/95	Japan			Abstract Only
	A17	WO 95/28929 A1	11/95	WO			
	A18	WO 96/29392 A1	09/96	WO			
	A19	WO 97/27851 A1	08/97	WO			
	A20	WO 98/57618 A1	12/98	WO			
	A21	JP 11029430	02/99	Japan			Abstract Only
	A22	JP 11029307	02/99	Japan			Abstract Only
	A23	WO 99/65889 A1	12/99	WO			

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

A24	Allison, D.G. et al., "A staining technique for attached bacteria and its correlation to extracellular carbohydrate production", <i>J. Microbiol. Methods</i> , 2:93-99 (1984).
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Examiner	Date Considered
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO UIZ-068CP	SERIAL NO. 09/945325
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Pesci, Everett C. et al.	MAR 06 2003
		FILING DATE August 31, 2001	GROUP 1625 TECH CENTER 1600/290

O I P E FEB 21 2003

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)			
B1	B1A	Allison, D.G. et al., "The role of exopolysaccharides in adhesion of freshwater bacteria", <i>J. Gen. Microbiol.</i> , 133:1319-1327 (1987).	
B2		Ames, D.E. et al. "N-oxides of some hydroxy- and amino-quinolines," <i>Journal of the Chemical Society</i> , p.3079-3082 (1956).	
B3		Anwar, H. et al., "Dynamic interactions of biofilms on mucoid <i>Pseudomonas aeruginosa</i> with tobramycin and piperacillin", <i>Antimicrob. Agents Chemother.</i> , 36:1208-1214 (1992).	
B4		Bainton, N.J. et al., "A general role for the <i>lux</i> autoinducer in bacterial cell signalling: Control of antibiotic synthesis in <i>Erwinia</i> ", <i>Gene.</i> , 116:87-91 (1992).	
B5		Bainton, N.J. et al., "N-(3-oxohexaonyl)-L-homoserine lactone regulates carbepenem antibiotic production in <i>Erwinia carotovora</i> ", <i>Biochem. J.</i> , 288:997-1004 (1992).	
B6		Bayer, V. et al. "Synthese de F-Alkyl-2 chromones et mise en evidence de leurs intermediaires reactionnels," <i>Journal of Fluorine Chemistry</i> , 20:497-505 (1982). [French with English abstract.]	
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B8		Bever, et al., "Molecular Characterization and Nucleotide Sequence of the <i>Pseudomonas aeruginosa</i> Elastase Structural Gene," <i>Journal of Bacteriology</i> , 1988, vol. 170, No. 9, 4309-4314.	
B9		Boivin, J. et al., "Biodeterioration of Materials" In <i>Biodeterioration and biodegradation 8</i> (ed.) H.W. Rossmore, Elsevier Applied Science, London, pp. 53-62 (1991).	
B10		Bonini, B.F. et al. "Synthesis and properties of a new family of chiral mesogens containing the 2,3-dihydrobenzopyran nucleus," <i>J. Organ. Chem.</i> , 59:5930-5936 (1994).	
B11		Boyd, A. et al., "Sequence of the <i>algL</i> gene of <i>Pseudomonas aeruginosa</i> and purification of its alginic lyase product", <i>Gene</i> , 131:1-8 (1993).	
B12		Boyd, A. et al., "Role of alginic lyase in cell detachment of <i>Pseudomonas aeruginosa</i> ", <i>Appl. Environ. Microbiol.</i> , 60:2355-2359 (1994).	
B13		Brint, J.M. et al., "Synthesis of multiple exoproducts in <i>Pseudomonas aeruginosa</i> is under the control of RH1R-Rh1L. Another set of regulators in strain PAO1 with homology to the autoinducer-responsive LuxR-LuxI family", <i>J. Bacteriol.</i> , 177:7155-7163 (1995).	
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B15		Cao, J-G. et al., "Purification and Structural Identification of an Autoinducer for the Luminescence System of <i>Vibrio harveyi</i> " <i>Journal of Biological Chemistry</i> , 1989, vol. 264, No. 36, pp. 21670-21676	
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B17		Chapon-Hervé, C. et al. "Regulation of the <i>xcp</i> secretion pathway by multiple quorum-sensing modulons in <i>Pseudomonas aeruginosa</i> ", <i>Molecular Microbiology</i> 24(6):1169-78 (1997).	
B18		Choi, S.H. et al., "Genetic Dissection of DNA Binding and Luminescence Gene Activation by the <i>Vibrio fischeri</i> LuxR Protein," <i>Journal of Bacteriology</i> , 1992, vol. 174, No. 12, 4064-4069.	
B19		Christensen, B.E. et al., "Physical and chemical properties of biofilms", In: Characklis, W.G. et al (eds.) <i>Biofilms</i> . John Wiley & Sons, New York, pp. 93-130 (1990).	

Examiner	Date Considered
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO UIZ-068CP	SERIAL NO. 09/945325
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Pesci, Everett C. et al.	MAR 06 2003 RECEIVED U.S. PATENT & TRADEMARK OFFICE TECH CENTER 1600, 2900 1625
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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

C1	Cohen-Bazire, G. et al., "Kinetic studies of pigment synthesis by non-sulfur purple bacteria", <i>J. Cell. Comp. Physiol.</i> , 49:25-68 (1957).
C2	Coppola, G.M. "The chemistry of 2H-3,1-benzoxazine-2,4(1H)-dione (isatoic anhydride). 17[1]. Synthesis of 2-Alkyl-4-quinolone alkaloids via a one-step reaction of N-methylisatoic anhydride with methyl ketone enolates," <i>Journal of Heterocyclic Chemistry</i> 22(3):491-494 (1985).
C3	Cornforth, J.W. et al. "Structure of a naturally occurring antagonist of dihydrostreptomycin", <i>The Biochemical Journal</i> , 63:124-130 (1956).
C4	Costerton, J.W. et al., "Bacterial biofilms in nature and disease", <i>Ann. Rev. Microbiol.</i> , 41:435-464 (1987).
C5	Davies, D.G. et al., "Exopolysaccharide production in biofilms: Substratum activation of alginate gene expression by <i>Pseudomonas aeruginosa</i> ", <i>Appl. Environ. Microbiol.</i> , 59:1181-1186 (1993).
C6	Davies, D.G. et al., "Regulation of the alginate biosynthesis gene <i>algC</i> in <i>Pseudomonas aeruginosa</i> during biofilm development in continuous culture", <i>Appl. Environ. Microbiol.</i> , 61:860-867 (1995).
C7	DeKievit, T.R. et al., "Quorum sensing, gene expression and <i>Pseudomonas</i> biofilms", <i>Methods in Enzymology</i> 310:117-128 (Sep 1999).
C8	Dempsey, M.J., "Marine bacterial fouling: A scanning electron microscope study", <i>Marine Biol.</i> , 61:305-315 (1981).
C9	Eberhard, A. et al., "Structural identification of autoinducer of <i>Photobacterium fischeri luciferase</i> ", <i>Biochemistry</i> , 20:2444-2449 (1981).
C10	Eberhard, A. et al., "Analogs of the autoinducer of bioluminescence in <i>Vibrio fischeri</i> ", <i>Arch. Microbiol.</i> , 146:35-40 (1986).
C11	Eberhard, et al., "Synthesis of the <i>lux</i> gene autoinducer in <i>Vibrio fischeri</i> is positively autoregulated," <i>Archives of Microbiology</i> , 1991, vol. 155, 294-297.
C12	EMBL accession no. AF004504 for "Pseudomonas aeruginosa pyocyanine biosynthesis operon, complete sequence (4 Jul 1997).
C13	Finlay, B.B. et al., "Common themes in microbial pathogenicity", <i>Microbiol. Rev.</i> , 53:210-230 (1989).
C14	Fletcher, M. "Adherence of marine micro-organisms to smooth surfaces", pp. 347-374. In Beachey, E.H. (ed.), <i>Bacterial Adherence (receptors and recognition, series 3 vol. 6.)</i> Chapman & Hall, London (1980).
C15	Floodgate, G.D. "The mechanism of bacterial attachment to detritus in aquatic systems", <i>Memorie dell'Istituto Italiano di idrobiologica Dott. Carco di Marchi</i> 29 (suppl.), 311-323 (1972).
C16	Fuqua, W.C. et al. "Quorum sensing in bacteria: The luxR-luxI family of cell density-responsive transcriptional regulators", <i>J. Bacteriol.</i> , 176:269-275 (1994).

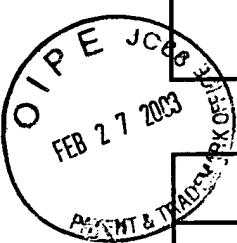
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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)		
	D1	Gacesa, P., "Alginate-modifying-enzymes. A proposed unified mechanism of action for the lyases and epimerases", <i>FEBS Lett.</i> , 212:199-202 (1987).
	D2	Gambello, M.J. et al., "Cloning and Characterization of the <i>Pseudomonas aeruginosa lasR</i> Gene, a Transcriptional Activator of Elastase Expression," <i>Journal of Bacteriology</i> , 1991, vol. 173, No. 9, 3000-3009.
	D3	Gambello, M.J. et al., "LasR of <i>Pseudomonas aeruginosa</i> is a transcriptional activator of the alkaline protease gene (<i>apr</i>) and an enhancer of exotoxin A expression", <i>Infect. Immun.</i> , 61:1180-1184 (1993).
	D4	Geesey, G.G. et al., "Microscopic examination of natural sessile bacterial populations from an alpine stream", <i>Can. J. Microbiol.</i> , 23:1733-1736 (1997).
	D5	Givskov, M. et al., "Eukaryotic interference with homoserine lactone-mediated prokaryotic signalling", <i>J. Bacteriol.</i> , 178:6618-6622 (1996).
	D6	Goswami, A. et al., "Microbial Hydroxylation of Quadrone to 8a-Hydroxyquadrone," <i>Journal of Natural Products</i> , 1987, vol. 50, No. 1, 49-54.
	D7	Guilhon, G.M.S.P. et al., "2-alkyl-4-quinolone alkaloids and cinnamic acid derivatives from <i>Esenbeckia almawillia</i> " <i>Phytochemistry</i> , 37(4):1193-1195.
	D8	Hengge-Aronis, R., "Survival of hunger and stress: The role of <i>rpoS</i> in early stationary phase regulation in <i>E. coli</i> ", <i>Cell</i> , 72:165-168 (1993).
	D9	Hirao, I. et al. "A convenient synthesis of 2- and 2,3-substituted 4H-chromen-4-ones," <i>Synthesis</i> , 22:1076-1078.
	D10	Høiby, N. "Pseudomonas Aeruginosa Infection in Cystic Fibrosis," <i>Acta. Path. Microbiol. Scand. Sect. B.</i> , 1974, vol. 82, 551-558.
	D11	Holloway, B.W., "Genetic recombination in <i>Pseudomonas aeruginosa</i> ", <i>J. Gen. Microbiol.</i> , 13:572-581 (1955).
	D12	Iglewski, B.H. et al., "NAD-Dependent Inhibition of Protein Synthesis by <i>Pseudomonas aeruginosa</i> Toxin," <i>PNAS</i> , 1975, vol. 72, 2284-2288.
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	D15	Jones, S. et al., "The lux autoinducer regulates the production of exoenzyme virulence in <i>Erwinia carotovora</i> and <i>Pseudomonas aeruginosa</i> ," <i>EMBO Journal</i> , 1993, vol. 12, No. 6, 2477-2482.
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	D17	Kessler, E. et al., "Synthesis, Processing and Transport of <i>Pseudomonas aeruginosa</i> Elastase," <i>Journal of Bacteriology</i> , 1988, vol. 170, No. 11, 5241-5247.
	D18	Khoury, A.E. et al., "Prevention and control of bacterial infections associated with medical devices", <i>ASAIO J.</i> , 38:M174-M178 (1992).
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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

	E1	Kostova, I. et al. "Alkaloids and coumarins from <i>Ruta graveolens</i> ", <i>Monatshefte für Chemie</i> , 130(5):703-707 (1999).
	E2	Latifi, A. et al., "Multiple homologues of LuxR and LuxI control expression of virulence determinants and secondary metabolites through quorum sensing in <i>Pseudomonas aeruginosa</i> PAO1", <i>Mol. Microbiol.</i> , 17:333-343 (1995).
	E3	Latifi, A. et al., "A hierarchical quorum sensing cascade in <i>Pseudomonas aeruginosa</i> links the transcriptional activators lasR and RhlR (VsmR) to expression of the stationary-phase sigma factor RpoS", <i>Mol. Microbiol.</i> , 21:1137-1146 (1996).
	E4	Meighen, E.A. "Molecular Biology of Bacterial Bioluminescence," <i>Microbiological Reviews</i> , 1991, vol. 55, No. 1, 123-142.
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	E6	Nichols, W.W. et al., "The penetration of antibiotics into aggregates of mucoid and non-mucoid <i>Pseudomonas aeruginosa</i> ", <i>J. Gen. Microbiol.</i> , 135:1291-1303 (1989).
	E7	Ochsner, U.A., et al., "Autoinducer-mediated regulation of rhamnolipid biosurfactant synthesis in <i>Pseudomonas aeruginosa</i> ", <i>PNAS USA</i> , 92:6424-6428 (1995).
	E8	Passador, L. et al., "Expression of <i>Pseudomas aeruginosa</i> Virulence Genes Requires Cell-to-Cell Communication," <i>Science</i> , 1993, vol. 260, 1127-1129.
	E9	Passador, L. et al., "Functional analysis of the <i>Pseudomonas aeruginosa</i> autoinducer PAI", <i>J. Bacteriology</i> , 1996, 5995-6000.
	E10	Pearson, J.P. et al., "Structure of the autoinducer required for expression of <i>Pseudomonas aeruginosa</i> virulence genes," <i>PNAS USA</i> , 1994, vol. 91, No. 1, 197-201.
	E11	Pearson, J.P. et al., "Roles of <i>Pseudomonas aeruginosa</i> las and rhl quorum-sensing systems in control of elastase and rhamnolipid biosynthesis genes" <i>Journal of Bacteriology</i> 179(18):5756-5767 (Sep 1997).
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